August 5, 2005

Gail M. Garvin
Global Environmental, Health & Safety Specialist
Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268

Dear Ms. Garvin:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2-chloro-5-trichloromethylpyridine posted on the ChemRTK HPV Challenge Program Web site on March 5, 2004. I commend Dow AgroSciences LLC for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Dow AgroSciences advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: M. E. Weber
N. Patel
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
2-Chloro-5-trichloromethylpyridine

Summary of EPA Comments

The sponsor, Dow AgroSciences LLC, submitted a test plan for 2-chloro-5-trichloromethylpyridine (CTCMP; CAS No. 69045-78-9) on December 31, 2003; the sponsor submitted robust summaries to EPA for CTCMP on September 24, 2004. EPA posted the test plan submission on the ChemRTK HPV Challenge Web site on March 5, 2004. Robust summaries were also submitted for the proposed analog; 2,3,4,5,6-pentachloropyridine (PCP; CAS No. 2176-62-7).

EPA has reviewed this submission and has reached the following conclusions:

1. Analog Justification. PCP is not an adequate analog for CTCMP.

2. Physicochemical Properties. The submitted data for melting point, partition coefficient and water solubility are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured values for boiling point and vapor pressure.

3. Environmental Fate. The submitted biodegradation data are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide photodegradation, stability in water, and fugacity data for this chemical as well as additional information from the biodegradation study.

4. Health Effects. The submitted data for acute effects are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide data on CTCMP for all other health effects endpoints; the claim of reduced-testing status is inadequately supported.

5. Ecological Effects. The submitted data for fish and invertebrates are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide algal toxicity data on CTCMP.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the 2-Chloro-5-trichloromethylpyridine
Challenge Submission

Test Plan

Analog Justification

The submitter provided robust summaries for PCP as well as for CTCMP, stating that quantitative structure-activity relationships comparing the two chemicals in conjunction with the robust summaries would satisfy the requirements of the HPV Chemical Challenge Testing Program. However, the submitter provided no rationale for the use of PCP as a structural analog of CTCMP. Further, EPA believes that there will be significant differences in physicochemical properties and toxicity between CTCMP and PCP given the different substituents and substitution patterns. The fish and daphnia toxicity values submitted for PCP and CTCMP do differ significantly.

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data for melting point, partition coefficient and water solubility are adequate for the purposes of the HPV Challenge Program.

Boiling Point. The calculated boiling point value provided is inadequate because it is below 300 °C. The submitter needs to provide measured data for this endpoint following OECD TG 103.

Vapor Pressure. The calculated vapor pressure data provided are inadequate because it is above 1×10^{-5} Pa. The submitter needs to provide measured data for this endpoint following OECD TG 104.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitted biodegradation data are adequate for the purposes of the HPV Challenge Program.

Photodegradation and fugacity. The submitter needs to provide data on CTCMP for these endpoints.

Stability in water. The submitter needs to provide stability in water data for CTCMP following OECD TG 111.

Biodegradation. The submitter needs to add certain information from the study that is relevant to ready biodegradability (see Specific Comments on the Robust Summaries, below; see also OECD TG 301).

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitted data for acute effects are adequate for the purposes of the HPV Challenge Program.

Genetic Toxicity. The submitter needs to provide *in vitro* testing data for gene mutations and chromosomal aberrations according to OECD TGs 471 and 473.

Repeated-Dose Toxicity. The two submitted 14-day inhalation studies on CTCMP are of shorter duration than 28 days and therefore are not adequate to address the repeated-dose toxicity endpoint for the purposes of the HPV Challenge Program.

The submitter states that the sponsored substance is a “site-limited intermediate” and is thus eligible for reduced health effects testing. However, the level of information provided in the test plan is not sufficient to support a closed-system intermediate (CSI) claim under the HPV Challenge Program (see guidance at http://www.epa.gov/chemrtk/closed9.htm).

The information required to support a CSI claim must address the following:

I. Site information
    A. Number of sites.
    B. Basis for “closed process” conclusion at each site.
        1) Process description.
        2) Monitoring data showing no detection.
        3) In the absence of monitoring data, the basis for believing that releases do not occur.
    C. Data on “presence in distributed products.”
II. Information on transport (mode, volume, controls, etc)
III. A data search showing that the chemical is not present in other end products.

Unless adequate additional information is provided to support the CSI claim, the submitter needs to address the repeated-dose toxicity and reproductive toxicity endpoints. EPA recommends a combined repeated-dose/reproductive/developmental toxicity screening test according to OECD TG 422.

Reproductive/Developmental Toxicity. The submitter needs to provide data for the reproductive/ developmental toxicity endpoints. EPA recommends a combined repeated-dose/reproductive/ developmental toxicity screening test according to OECD TG 422 to address these endpoints. If the submitter provides adequate support for the CSI claim, a reproductive/developmental toxicity screening test according to OECD TG 421 will satisfy the developmental toxicity endpoint.

Ecological Effects (fish, invertebrates, and algae)

The submitted data for fish and invertebrate acute effects are adequate for the purposes of the HPV Challenge Program.

Algae. The submitter needs to provide data on CTCMP for algae according to OECD TG 201.

Specific Comments on the Robust Summaries

Environmental Fate

Biodegradation. The submitter needs to include the following information: initial concentration of the test material, temperature of incubation and test results expressed as percentage biodegradation.

Ecological Effects

The robust summary titles for fish and invertebrates are reversed and should be corrected.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.